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Attorney Docket No.: 00.22US

PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of: Maes, et al.

Serial No.: 09/773,351

Group Art Unit: 1619

Filed: January 31, 2001

Examiner: Willis, M.

For: Cholesterol Sulfate and Amino Sugar Compositions for Enhancement of Stratum Corneum Function

RESPONSE PURSUANT TO 37 CFR 1.111

The Assistant Commissioner of Patents and Trademarks

Washington, D.C. 20231

Dear Sir:

In response to the Examiner's Final Action dated December 12, 2001, please enter the following amendment and consider the following remarks which are believed to place the application in condition for allowance or in better condition for appeal in the event the final rejection is maintained.

CLEAN AMENDMENTS

Please amend the following claim as follows in its clean form below and as the previous version of the claim is marked on the attached page entitled **MARKED AMENDMENTS.**

18 (Amended). The method of claim 16 in which the composition comprises about 0.04 to about 1.0 percent cholesterol sulfate.

REMARKS

I. Non-essential Material

The Examiner has stated in the previous Office Action that an amendment to the disclosure to include the material incorporated by reference is required because the incorporation of essential material is improper at page 2, second full paragraph. At this cite, it is disclosed that cholesterol sulfate is known to retard desquamation in the stratum corneum of the skin in PCT Publication No. WO00/45786. Applicants contend that the incorporation by reference of this publication is of non-essential subject matter related solely to the background of the invention. As permitted according to the MPEP 608.01(p), nonessential subject matter is information referred to for purposes of indicating the background of the invention or illustrating the state of the art. The present invention relates to a combination of cholesterol sulfate with an exfoliant, and the application of this combination to the skin is surprisingly effective in

strengthening the protective lipid barrier of the stratum corneum. However, because the present invention relates to a mixture of components, the background of each of the components individually is provided in the background section of the present specification. Thus, the mention of the PCT Publication addressing cholesterol sulfate in the background section is not essential material, and Applicants request that this objection be withdrawn.

II. 35 U.S.C. §112

The Examiner previously rejected claims 12, 18, and 20 under section 112, second paragraph for failing to particularly point out and distinctly claim the subject matter of the present invention. The Examiner suggested that this rejection can be overcome by adding the phrase "bark extract" to these claims. In Applicants' response of October 2, 2001, claims 12 and 20 were amended to add the word "extract." Support for these amendments is found in the present specification at page 7, lines 1 to 13. In this section of the specification the use of white birch is described and white birch bark extract is also set forth as the preferred protease inhibitor. Therefore, as amended, the claims of the present invention sufficiently point out and distinctly claim the white birch extract of the present invention, and Applicants request that this rejection be withdrawn.

The Examiner rejected claim 18 because it is a method claim depending from a composition claim. Applicants amend claim 18 herein to correct the inadvertent typographical errors in claim 18, including the claim number. Claim 18 should depend from claim 16 which is a method claim. Finally, claim 20 was also rejected by the Examiner as a result of typographical errors. Previously, in Applicants response of October 2, 2001, claim 20 was amended to remove the duplicate "of the" in the claim. Therefore, Applicants request that these rejections be withdrawn.

The Examiner rejected claim 19 under section 112, first paragraph for failing to describe subject matter such that one of ordinary skill in the art would be enabled to make and/or use the present invention. However, the enablement requirement of §112 has been interpreted to be an objective requirement, and therefore, this teaching can be provided through broad terminology or illustrative examples. *In re Wright*, 27 USPQ2d 1510, 1513 (CAFC 1993)(citing *In re Marzocchi*, 439 F.2d 220, 223, 169 USPQ 367, 369 (CCPA 1971); *In re Wands*, 858 F.2d 731, 736-37, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)). Thus, Applicants contend that the term "preventing" as used in claim 19 in connection with the description provided in the present specification is sufficient to enable one of ordinary skill in the art to make and/or use the present invention. As described at page 3, lines 13 to 15, the ability of the

present invention to prevent damage to the skin, especially when such damage is associated with a reduction or a loss of skin barrier function, is derived from the reparative and healing properties of the skin. This is further described in the present specification at page 3, lines 26 to 28, wherein it is explained that the appearance of fine lines and wrinkles can be prevented by maintaining a thicker stratum corneum. This is a key function of the present invention and is based on the logistical behavior of the stratum corneum that is readily observed by one of ordinary skill in the art.

Fine lines and wrinkles that are present on the surface of thinned skin are part of the process of aging and is an expected development especially if there is no treatment applied to the skin to prevent it. It well known that youthful skin (e.g. 15 to 25 years of age) has a thicker and suppler consistency than older skin (e.g., 30 to 60 years of age). Thus, if the surface thickness can be maintained, the wrinkles associated with the thinning of the skin can be prevented. As disclosed in the present specification of page 4, lines 14 to 17, the present invention achieves a thicker layer of the stratum corneum while still promoting the cycle of removing dead skin cell layers. As a result, moisture is retained, the skin is firmer, and the appearance of lines and wrinkles are prevented. Finally, at page 8, lines 2 to 13, of the present specification, the method of using the present invention to prevent damage to skin that has experienced a reduction or loss in barrier function is provided. In addition, in Example 1 at pages 8 to 10, the present specification demonstrates an 88 percent barrier repair over a placebo, indicating an improvement in the barrier function of the skin and prevention of damage. Therefore, the present specification fully enables one of ordinary skill in the art to prevent damage to the skin as described in claim 19.

Applicants also submit herewith several examples of recently issued patents containing claims "preventing" various conditions. The first two patents, U.S. Patent Nos. 6,262,050 (copies of cover page and columns 7 to 10), and 6,333,042 (copies of cover page and columns 9 to 14), provide examples of claims to prevent irritation or skin pain. The third patent, US 6,329,369 ("the '369 patent") (copies of cover page and columns 83 and 84) provides an example of the understanding that one of ordinary skill in the art has with respect to the reduction of a symptom as being indicative of "preventing" a condition. In the present situation, a inverse measurement is made of the damage by measuring the increase in the health of the skin based on the increased barrier repair, rather than the decrease in the damage. Nonetheless, in either case, i.e., measuring an increase in the positive condition or measuring a decrease in the negative condition, the measurement indicates the ability to prevent a symptom. In the case of the present invention, the symptom is damage to the skin, especially skin that has experienced a reduction in

its protective barrier. One of ordinary skill in the art would understand that an increase in the protective barrier correlates to preventing the damaging effects seen on the skin for the reasons explained above, and as explained in the present specification. Therefore, Applicants respectfully request that the Examiner's rejections based on lack of enablement under 35 U.S.C. §112, first paragraph be withdrawn.

III. Non-Obvious

The Examiner maintains in the final office that Ribier et al. (U.S. Patent No. 5,650,166; "the '166 reference") in view of Subbiah (U.S. Patent No. 6,150,381; "the '381 reference") renders claims 1 to 20 of the present invention obvious under 35 U.S.C. §103(a) because a mixture includes random solutions and vesicles. However, there is no support provided to indicate why or how one of ordinary skill in the art would understand that a mixture of the present invention is taught or suggested by a lipid vesicle described in the '166 reference. To establish a *prima facie* case of obviousness based on a combination of the content of various references, there must be some teaching, suggestion or motivation in the prior art to make the specific combination that was made by the applicant. *In re Raynes*, 7 F.3d 1037, 1039, 28 USPQ2d 1630, 1631 (Fed. Cir. 1993); *In re Oetiker*, 977 F.2d 1443, 1445, 24 USPQ2d 1443, 1445 (Fed. Cir. 1992). There is no teaching, suggestion or motivation in the art or the knowledge of one of ordinary skill in the art to support the assertion that mixing components is equivalent to or includes encapsulating components. Moreover, cited '166 reference demonstrates just the opposite: that specific processing steps required to make a vesicle distinguish it from a mixture.

One of ordinary skill in the art understands the difference between a mixture of components, a random solution of components, and a vesicle, a discrete arrangement of its components. Evidence of this is found in the cited references wherein specific processing steps to make a lipid vesicle are taught and/or suggested at column 7, line 42 "A) Production of lipid vesicles containing ASL" to column 8, line 4 "B) Production of the cosmetic composition." The process of making lipid vesicles includes, for example, evaporation or co-fusion to achieve encapsulation. This is in stark contrast to the present invention of a simple mixture of an effective amount of an exfoliant and cholesterol sulfate. The combination of these two components has surprisingly been found to improve and/or protect the barrier of the stratum corneum even though the two components have opposite acting activities with respect to exfoliation. The present invention is not taught or suggested by the cited references nor would one of ordinary skill in the art reasonably expect to achieve the present invention based on the combination of the '742 reference and the '381 reference as discussed in further detail below.

The '381 reference teaches sclareolide-like compounds for treating disorders caused by microbials such as, for example, bacteria, and one specific disorder is acne. The '381 topical formulations containing sclareolide are generally prepared, according to the '381 reference, by admixing sclareolide in water and at least one organic solvent. Therefore, the '381 reference teaches that sclareolide is an aqueous active. Thus, the combination of the '381 reference with the '166 reference fails to teach or suggest the present invention because one of ordinary skill in the art would expect the sclareolide disclosed in the '381 reference to be incorporated within the aqueous cavity of the lipid vesicles disclosed by the '166 reference, and therefore, be encapsulated. The '166 references teaches a moisturizing composition which comprises a first and a second dispersion of lipid vesicles. The '166 reference discloses at column 3, lines 66 to 67, that the lipid phase of the vesicles is an alkali metal salt of cholesterol sulphate. Therefore, the alkali metal salt of cholesterol sulphate is disclosed as part of the lipid bilayer which forms the cavity within which an aqueous active, i.e., sclareolide, is encapsulated. This is not a mixture of cholesterol sulphate and an exfoliant as is the subject of the present invention, and therefore, the combination of the '381 reference and the '166 reference fails to teach or suggest the present invention.

In the final action, the Examiner also asserts that the feature of a mixture is not recited in the claims nor is it taught in the specification. However, Applicants contend that a mixture is taught both in the claims and the specification. First, at page 3, lines 5 to 6, the invention is described as being a topically applied composition that is a mixture of an exfoliant and a cholesterol sulfate. Further on page 3, at lines 18 to 20, the present invention described as a cholesterol sulfate and an exfoliant combined in a mixture. Again at page 4, line 25, the components of the mixture are described throughout the paragraph. Finally, at page 5, lines 12 to 13, cited by the Examiner, the combination of the two components have previously been described as a mixture, as it has been pointed out at pages 3 and 4. Thus, the combination refers to the mixture previously mentioned and described in further detail on pages 3 and 4. In addition, the "combination" that can be applied in any type of vehicle refers to the mixture previously described in the specification. Further evidence that the reference to a combination would be understood as a mixture is found in the following paragraph on page 5, lines 20 to 25, wherein the mixture is specifically stated as being used in therapeutic products as well as color cosmetic products. Therefore, a mixture is taught in the present specification and one of ordinary skill in the art would understand that the teachings in the present specification are to mixtures and not lipid vesicles.

In addition to teaching a mixture in the present specification, the claims specifically state a mixture. Claims 1, 13, 16 and 19 each describe a composition comprising a mixture of cholesterol sulfate and an exfoliant. As previously elaborated upon, the steps taken to make a mixture and the steps taken to make a lipid vesicle are vastly different, and the resulting products, i.e, a mixture versus a vesicle, are as vastly different as their processing steps. Therefore, the combination of the '166 reference and the '381 reference fails to teach or suggest the mixture of the present invention and fails to teach or suggest the beneficial results derived from the simple mixture of the present invention. Because none of the cited references alone nor in combination would lead one of ordinary skill in the art to the compositions and methods of the present invention, a *prima facie* case of obviousness has not been established. Applicants request therefore, that the Examiner's rejection under §103 be withdrawn.

CONCLUSION

In view of the arguments presented above in the present submission, the claims are believed to be in condition for allowance, and issuance of a Notice of Allowance is respectfully solicited.

Respectfully submitted,

March 12, 2002

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MARKED AMENDMENTS

18 (Amended). The method of claim [1] 16 in which the composition comprises about 0.04 to about 1.0 percent cholesterol sulfate.

US006329369B1

(12) United States Patent
Chow et al.

(10) Patent No.: US 6,329,369 B1
(45) Date of Patent: Dec. 11, 2001

(54) METHODS OF TREATING PAIN AND OTHER CONDITIONS

(75) Inventors: Ken Chow, Newport Coast; Daniel W. Gil, Corona Del Mar; James A. Burke, Santa Ana; Dale A. Harcourt, San Clemente; Michael E. Garst, Newport Beach; Larry A. Wheeler, Irvine, all of CA (US); Stephen A. Munk, Northville, MI (US)

(73) Assignee: Allergan Sales, Inc., Irvine, CA (US)

(*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 0 days.

(21) Appl. No.: 09/679,919

(22) Filed: Oct. 5, 2000

Related U.S. Application Data

(60) Division of application No. 09/329,752, filed on Jun. 10, 1999, now abandoned, which is a continuation-in-part of application No. 09/205,597, filed on Dec. 4, 1998, now abandoned, which is a continuation-in-part of application No. 08/985,347, filed on Dec. 4, 1997, now abandoned.

(51) Int. Cl.[7] A61R 31/4168; A61R 31/4178; A61R 31/538; A61N 9/02; A61N 11/02; A61N 27/06

(52) U.S. Cl. 514/230.5; 514/249; 514/255; 514/370; 514/377; 514/392; 514/397; 514/401; 514/413; 514/415; 514/816; 514/913; 514/230.8

(58) Field of Search 514/249, 377, 514/413, 415, 255, 816

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Primary Examiner—Floyd D. Higel
(74) *Attorney, Agent, or Firm*—Carlos A. Fisher; Robert J. Baran; Martin A. Voet

(57) ABSTRACT

Methods of treating glaucoma or elevated pressure and other diseases with reduced side effects by treating a mammal in need thereof an agonist of the alpha 2B or alpha 2B/2C adrenergic receptor(s). Also described are compounds having such selective agonist activity.

17 Claims, No Drawings

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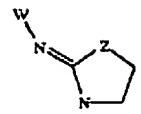
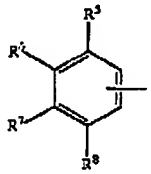


wherein W is a bicyclic radical selected from the group consisting of



wherein R^5, R^6, R^7 and R^8 are selected from the group consisting of H and lower alkyl provided that at least one of R^5 and R^6 or R^6 and R^7 are $OC(R^9)C(R^9)N(R)$ to form a condensed ring with

wherein R^9 is H, lower alkyl or oxo and

wherein R^{10} is H, lower alkyl, phenyl or lower alkyl substituted phenyl, and Z is O or NH.

9. A process of claim 8 wherein the agonist has an efficacy at least about 0.3 greater at the α2B or 2C adrenoceptor subtypes than at the α2A adrenoceptor subtype, and wherein its efficacy at the α2A adrenoceptor subtype is ≦0.4.

10. A process of claim 9 wherein approximately 0.001% to 5% by weight of the agonist is administered topically to the mammal in daily or twice daily doses.

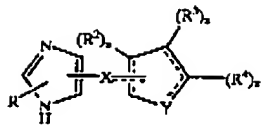
11. A process of claim 10 wherein approximately 0.01% to 3.0% by weight of the agonist is administered topically to the mammal in daily or twice daily doses.

12. A process of claim 8 wherein said agonist has no detectable activity at the α2A adrenoreceptor subtypes.

13. A process of claim 8 wherein said agonist has no detectable activity at the α2A and α2C adrenoreceptor subtypes.

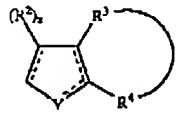
14. A process for administering to a mammal a pharmaceutical composition comprising a therapeutically effective dose of a compound to treat or prevent a pathological condition selected from the group consisting of muscle spasticity; pain; neurodegenerative diseases, spinal ischemia and stroke; memory and cognition deficits; psychoses, anxiety and depression; hypertension; congestive heart failure; cardiac ischemia and nasal congestion, wherein said compound has adrenergic activity and is a selective agonist of the α2B or α2B/α2C adrenoceptor receptor subtype(s), said selective agonist having a structure selected from the group consisting of compounds having the formula

I



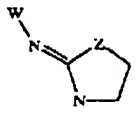
wherein the dotted lines represent optional double bonds; R is H or lower alkyl; X is S or $C(H)R^1$, wherein R^1 is H or lower alkyl or R^1 is absent when X is S or when the bond between X and the ring represented by

is a double bond; Y is O, N, S, $(CR^1x)_y$, wherein y is an integer of from 1 to 3, —CH=CH— or $—Y^1CH_2—$, wherein Y^1 is O, N or S; x is an integer of 1 or 2, wherein x is 1 when R^2, R^3 or R^4 is bound to an unsaturated carbon atom and x is 2 when R^2, R^3 or R^4 is bonded to a saturated carbon atom; R^2 is H, lower alkyl, halogen, hydroxy or lower alkoxy, or oxo; R_3 and R^4 are, each, H, lower alkyl, hydroxy, lower alkoxy, or phenyl or, together, are $—(C(R^2)x)z—$; $—Y^1(C(R^2)x)z'—$; $—Y^1(C(R^2)x)y\ Y^1—$; $—(C(R^2)x)—Y^1—(C(R^2)x)—$; $—(C(R^2)x)—Y^1—(C(R^2)x)—(C(R^2)x)—$ and $—Y^1—(C(R^2)x)—Y^1—(C(R^2)x)—$ wherein z is an integer of from 3 to 5, z' is an integer of from 2 to 4 and x and y are as defined above, and further either end of each of these divalent moieties optionally attach at either R^3 or R^4 to form the condensed ring structure

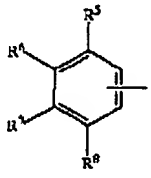


and the ring thus formed is totally unsaturated, partially unsaturated, or totally saturated provided that a ring carbon has no more than 4 valences, nitrogen no more than three and O and S have no more than two; or

V



wherein W is a bicyclic radical selected from the group consisting of



wherein R^5, R^6, R^7 and R^8 are selected from the group consisting of H and lower alkyl provided that at least one of

US006262050B1

(12) **United States Patent**
De Lacharriere

(10) **Patent No.: US 6,262,050 B1**
(45) **Date of Patent: Jul. 17, 2001**

(54) **TOPICAL COMPOSITION CONTAINING CAPSAZEPINE**

(75) Inventor: **Olivier De Lacharriere**, Paris (FR)

(73) Assignee: **Societe l'Oreal S.A.**, Paris (FR)

(*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 0 days.

(21) Appl. No.: **09/457,667**

(22) Filed: **Dec. 9, 1999**

Related U.S. Application Data

(63) Continuation of application No. 09/068,237, filed as application No. PCT/FR96/01592 on Oct. 11, 1996, now Pat. No. 6,048,855.

(30) **Foreign Application Priority Data**

Nov. 6, 1995 (FR) 95/13196

(51) **Int. Cl.**[7] **A01N 43/46**; A61K 31/55
(52) **U.S. Cl.** **514/213.01**
(58) **Field of Search** 514/213

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Primary Examiner—Dwayne C. Jones
(74) *Attorney, Agent, or Firm*—Burns, Doane, Swecker & Mathis, L.L.P.

(57) **ABSTRACT**

A topical composition containing capsazepine and particularly suitable for treating neurogenic skin disorders and diseases, especially painful and/or pruriginous diseases, as well as for treating sensitive skin and eyes, in particular, the composition is useful for preventing and/or controlling skin and/or eye irritation, itching, erythema and dysaesthesia and heating of the skin, eyes and mucosa, as well as for reducing the irritancy of an active substance having an irritant side-effect.

9 Claims, No Drawings

-continued

Polysorbate 60 (Tween 60, sold by the Company ICI)		1.00
Stearic acid		1.40
Triethanolamine		0.70
Carbomer		0.40
Liquid fraction from karite butter		12.00
Perhydrosqualene		12.00
Antioxidant		0.05
Fragrance		0.5
Preservative		0.30
Water	q.s. for	100%

EXAMPLE 3

Shampoo

Sodium magnesium lauryl ether sulphate containing 4 mol of ethylene oxide, sold under the name of Texapon ASV by Henkel (anionic surfactant)		6.50
Capsazepine		0.02
Hydroxypropylcellulose (Klucel H, sold by the Company Hercules)		1.00
Fragrance		0.50
Preservative		0.30
Water	q.s. for	100%

EXAMPLE 4

Anti-wrinkle care cream for the face (oil-in-water emulsion)

Capsazepine		0.03
Glyceryl stearate		2.00
Polysorbate 60 (Tween 60, sold by the Company ICI)		1.00
Stearic acid		1.40
5-(n-Octanoyl)salicylic acid		0.50
Triethanolamine		0.70
Carbomer		0.40
Liquid fraction from karite butter		12.00
Perhydrosqualene		12.00
Antioxidant		0.05
Fragrance		0.5
Preservative		0.30
Water	q.s. for	100%

EXAMPLE 5

Emulsified gel for the care of insect stings (oil-in-water emulsion)

Cyclomethicone		3.00
Purcellin oil (sold by the Company Dragoco)		7.00
PEG-6/PEG-32/Glycol stearate (Tefose ® 63 from Gattefosse)		0.30
Capsazepine		
Preservative		0.15
Fragrance		0.40
Carbomer		0.60
Crotamiton		5.00
Glycyrrhetinic acid		3.00
Ethyl alcohol		5.00
Triethanolamine		0.20
Water	q.s. for	100%

EXAMPLE 6

Pain-control gel, in particular for the pain associated with shingles

Capsazepine		0.30
Hydroxypropylcellulose (Klucel H, sold by the Company Hercules)		1.00
Antioxidant		0.05
Lidocaine hydrochloride		2.00
Isopropanol		40.00
Preservative		0.30
Water	q.s. for	100%

EXAMPLE 7

Face cream for the care of rosacea (oil-in-water emulsion)

Capsazepine		0.25
Glyceryl stearate		2.00
Polysorbate 60 (Tween 60, sold by the Company ICI)		1.00
Stearic acid		1.40
Metronidazole		1.00
Triethanolamine		0.70
Carbomer		0.40
Liquid fraction from karite butter		12.00
Liquid petrolatum		12.00
Antioxidant		0.05
Fragrance		0.5
Preservative		0.30
Water	q.s. for	100%

EXAMPLE 8

Cream for caring for sensitive skins with respect to sunburn (oil-in-water emulsion) or for treating the symptoms relating to shingles

Capsazepine		0.25
Glyceryl stearate		2.00
Polysorbate 60 (Tween 60, sold by the Company ICI)		1.00
Stearic acid		1.40
Glycyrrhetinic acid		2.00
Triethanolamine		0.70
Carbomer		0.40
Liquid fraction from karite butter		12.00
Sunflower oil		10.00
Antioxidant		0.05
Fragrance		0.5
Preservative		0.30
Water	q.s. for	100%

EXAMPLE 9

Ocular collyrium

Capsazepine		0.03
Excipient	q.s. for	100
Sodium chloride		
Sodium borate		
Polysorbate 80		
Boric acid		
Water		

What is claimed is:

1. A method for treating cutaneous pain, said method comprising topically applying an effective amount of cap-

sazepine to a patient in need of such treatment to prevent and/or combat cutaneous pain.

2. A method for treating cutaneous and/or ocular irritation, erythemas, pruritus or warming and/or dysaesthetic sensations of the skin, the eyes or mucous membranes, said method comprising topically applying an effective amount of capsazepine to a patient in need of such treatment to prevent and/or combat cutaneous and/or ocular irritation, erythema, pruritus or warming and/or dysaesthetic sensations of the skin or the eyes.

3. A method for treating symptoms related to shingles, eczema, sensitive skin or eyes, pruriginous diseases, pruritus, herpes, atopic or contact dermatitides, lichens, prurigos, insect stings, rosacea, conjunctivitis or uveitides, said method comprising topically applying an effective amount of capsazepine to a patient in need of such treatment to prevent and/or combat symptoms related to shingles, eczema, sensitive skin or eyes, pruriginous diseases, pruritus, herpes, atopic or contact dermatitides, lichens, prurigos, insect stings, rosacea, conjunctivitis or uveitides.

4. The method according to claim 1, wherein capsazepine is used in an amount ranging from 0.000001 to 5% by weight with respect to the total weight of the composition.

5. The method according to claim 2, wherein capsazepine is used in an amount ranging from 0.000001 to 5% by weight with respect to the total weight of the composition.

6. The method according to claim 3, wherein capsazepine is used in an amount ranging from 0.000001 to 5% by weight with respect to the total weight of the composition.

7. The method according to claim 4, wherein capsazepine is used in an amount ranging from 0.00001 to 0.5% by weight with respect to the total weight of the composition.

8. The method according to claim 5, wherein capsazepine is used in an amount ranging from 0.00001 to 0.5% by weight with respect to the total weight of the composition.

9. The method according to claim 6, wherein capsazepine is used in an amount ranging from 0.00001 to 0.5% by weight with respect to the total weight of the composition.

* * * * *

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De La Charriere et al.

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(45) Date of Patent: *Dec. 25, 2001

(54) **USE OF A SUBSTANCE P ANTAGONIST IN A COSMETIC COMPOSITION, AND THE COMPOSITION THUS OBTAINED**

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(*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 0 days.

This patent is subject to a terminal disclaimer.

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Related U.S. Application Data

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(30) **Foreign Application Priority Data**

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(58) **Field of Search** ..... 424/401, 49, 70.1, 424/59, 63, 76.1, DIG. 1; 514/15, 210, 293, 305, 315, 410, 416, 422, 844–848, 880, 881

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(57) **ABSTRACT**

A substance P antagonist is used in a cosmetic composition to treat sensitive skin. More specifically, a cosmetic composition containing a substance P antagonist is used to prevent and/or combat skin irritations, desquamation, erythermas, sensations of dysesthesia/overheating, or pruritus of the skin.

180 Claims, No Drawings

EXAMPLE 8

Shampoo

Sendide	0.003
Hydroxypropylcellulose (Klucel H, sold by the Hercules Company)	1.00
Perfume	0.50
Preservative	0.30
Water	qsp 100%

EXAMPLE 9

Emulsified Gel To Fight Insect Stings (Oil-in-water Emulsion)

Cyclomethicone	3.00
Purcellin oil (sold by the Dragoco Company)	7.00
PEG-6/PEG-32/Glycerol Stearate (Tefose 2 sold by Gattefosse)	0.30
Spantide II	0.02
Preservative	0.30
Perfume	0.40
Carbomer	0.60
Cetamiton	5.00
Glycyrrhetinic acid	2.00
Ethyl alcohol	5.00
Triethanolamine	0.20
Water	qsp. 100%

EXAMPLE 10

Pain-Fighting Gel

Spantide II	0.03
Hydroxypropylcellulose (Klucel H, sold by the Hercules Company)	1.00
Antioxidant	0.05
Lidocaine chlorhydrate	2.00
Isopropanol	40.00
Preservative	0.30
Water	qsp 100%

EXAMPLE 11

Anti-Acne Rosacea Face Cream (Oil-in-water Emulsion)

Spantide II	0.25
Glycerol stearate	2.00
Polysorbate 60 (Tween 60 sold by the ICI Company)	1.00
Stearic acid	1.40
Metronidazole	1.00
Triethanolamine	0.70
Carbomer	0.40
Liquid fraction of karite nut butter	12.00
Vaseline oil	12.00
Antioxidant	0.05
Perfume	0.50
Preservative	0.30
Water	qsp 100%

EXAMPLE 12

Anti-Solar Erythema Cream (Oil-in-water Emulsion)

Spantide II	0.25
Glycerol stearate	2.00
Polysorbate 60 (Tween 60 sold by the ICI Company)	3.00
Stearic acid	1.40
Glycyrrhetinic acid	2.00
Triethanolamine	0.70
Carbomer	0.40
Liquid fraction of karite nut butter	12.00
Sunflower oil	10.00
Antioxidant	0.05
Perfume	0.50
Preservative	0.30
Water	qsp 100%

What is claimed is:

1. A topically applicable cosmetic composition which is adapted for use in a cosmetic regimen that comprises topical application of said composition to at least one of the skin, hair, or mucous membranes, which composition comprises:

(1) an amount of at least one irritant substance sufficient to elicit an irritant side effect in a user having sensitive skin when utilized in a topical cosmetic regimen that does not include the use of a substance P antagonist, wherein said irritant substance is an active agent in said topical cosmetic regimen;

(2) an amount of at least one substance P antagonist sufficient to prevent or alleviate said irritation when said composition is utilized in a topical cosmetic regimen on a user having sensitive skin, wherein said substance P antagonist is a substance which possesses at least one of the following characteristics:

(i) it elicits a pharmacological response in at least one of the following tests:

(a) it reduces the extravasation of plasma through the vascular wall caused by capsaicin or antidromic nerve excitation; and

(b) it inhibits the contraction of smooth muscle induced by substance P; and

(3) a cosmetically acceptable medium.

2. A topically applicable cosmetic composition which is adapted for use in a cosmetic regimen that comprises topical application of said composition to at least one of the skin, hair, or mucous membranes, which composition comprises:

(1) an amount of at least one irritant substance sufficient to elicit an irritant side effect to a user having sensitive skin when utilized in a topical cosmetic regimen that does not include the use of a substance P antagonist, wherein said irritant substance is an active agent in said topical cosmetic regimen;

(2) an amount of at least one substance P antagonist sufficient to prevent or alleviate said irritation when said composition is utilized in a topical cosmetic regimen on a user having sensitive skin, wherein said substance P antagonist is a substance which possesses at least one of the following characteristics:

(i) it exhibits a selective affinity for the NK_1 receptors on the tachykinins; and

(ii) it elicits a pharmacological response in at least one of the following tests:

(a) it reduces the extravasation of plasma through the vascular wall caused by capsaicin or antidromic nerve excitation; and

(b) it inhibits the contraction of smooth muscle induced by substance P; and

(3) a cosmetically acceptable medium;

wherein said topically applicable cosmetic composition comprises a galenic formulation which is a solution or dispersion formulated as a lotion or serum, microgranulate dispersion, vesicular ionic or non-ionic dispersion, alcoholic or hydroalcoholic aqueous solution, cream, gel, oil-in-water or water-in-oil emulsion, foam, aerosol, solid or paste.

3. A topically applicable cosmetic composition which is adapted for use in a cosmetic regimen that comprises topical application of said composition to at least one of the skin, hair, or mucous membranes, which composition comprises:

(1) an amount of at least one irritant substance sufficient to elicit an irritant side effect to a user having sensitive skin when utilized in a topical cosmetic regimen that does not include the use of a substance P antagonist, and wherein said irritant substance is an active agent in said topical cosmetic regimen;

(2) an amount of at least one substance P antagonist sufficient to prevent or alleviate said irritation when said composition is utilized in a topical cosmetic regimen on a user having sensitive skin, wherein said substance P antagonist is a substance which possesses at least one of the following characteristics:

(i) it elicits a pharmacological response in at least one of the following tests:

(a) it reduces the extravasation of plasma through the vascular wall caused by capsaicin or antidromic nerve excitation; and

(b) it inhibits the contraction of smooth muscle induced by substance P; and

(3) a cosmetically acceptable medium;

wherein said topically applicable cosmetic composition suitable for use in a cosmetic regimen is selected from the group consisting of a hair care composition, skin care composition, cleansing composition, sunscreen composition, and a mouth care composition.

4. A topically applicable cosmetic composition which is adapted for use in a cosmetic regimen that comprises topical application of said composition to at least one of the skin, hair, or mucous membranes, which composition comprises:

(1) an amount of at least one irritant substance sufficient to elicit an irritant side effect to a user having sensitive skin when utilized in a topical cosmetic regimen that does not include the use of a substance P antagonist, and wherein said irritant substance is an active agent in said topical cosmetic regimen;

(2) an amount of at least one substance P antagonist sufficient to prevent or alleviate said irritation when said composition is utilized in a topical cosmetic regimen on a user having sensitive skin, wherein said substance P antagonist is a substance which possesses at least one of the following characteristics:

(i) it exhibits a selective affinity for the NK, receptors on the tachykinins; and

(ii) it elicits a pharmacolngical response in at least one of the following tests:

(a) it reduces the extravasation of plasma through the vascular wall caused by capsaicin or antidromic nerve excitation; and

(b) it inhibits the contraction of smooth muscle induced by substance P; and

(3) a cosmetically acceptable medium;

wherein said topically applicable cosmetic composition suitable for use in a cosmetic regimen is selected from the group consisting of a hair care composition, skin care composition, cleansing composition, sunscreen composition, and a mouth care composition.

5. A topically applicable cosmetic composition which is adapted for use in a cosmetic regimen that comprises topical application of said composition to at least one of the skin, hair, or mucous membranes, which composition comprises:

(1) an amount of at least one irritant substance sufficient to elicit an irritant side effect to a user having sensitive skin when utilized in a topical cosmetic regimen that does not include the use of a substance P antagonist, wherein said irritant substance is an active agent in said topical cosmetic regimen;

(2) an amount of at least one substance P antagonist sufficient to prevent or alleviate said irritation when said composition is utilized in a topical cosmetic regimen on a user having sensitive skin, wherein said substance P antagonist is a substance which possesses at least one of the following characteristics:

(i) it elicits a pharmacological response in at least one of the following tests:

(a) it reduces the extravasation of plasma through the vascular wall caused by capsaicin or antidromic nerve excitation; and

(b) it inhibits the contraction of smooth muscle induced by substance P; and

(3) a cosmetically acceptable medium;

wherein said topically applicable cosmetic composition comprises a galenic formulation which is a solution or dispersion formulated as a lotion or serum, microgranulate dispersion, vesicular ionic or non-ionic dispersion, alcoholic or hydroalcoholic aqueous solution, cream, gel, oil-in-water or water-in-oil emulsion, foam, aerosol, solid or paste.

6. A topically applicable cosmetic composition which is adapted for use in a cosmetic regimen that comprises topical application of said composition to at least one of the skin, hair, or mucous membranes, which composition comprises:

(1) an amount of at least one irritant substance sufficient to elicit an irritant side effect to a user having reactive skin when utilized in a topical cosmetic regimen that does not include the use of a substance P antagonist, wherein said irritant substance is an active agent in said topical cosmetic regimen;

(2) an amount of at least one substance P antagonist sufficient to prevent or alleviate said irritation when said composition is utilized in a topical cosmetic regimen on a user having reactive skin, wherein said substance P antagonist is a substance which possesses at least one of the following characteristics:

(i) it elicits a pharmacological response in at least one of the following tests:

(a) it reduces the extravasation of plasma through the vascular wall caused by capsaicin or antidromic nerve excitation; and

(b) it inhibits the contraction of smooth muscle induced by substance P; and

(3) a cosmetically acceptable medium.

7. A topically applicable cosmetic composition which is adapted for use in a cosmetic regimen that comprises topical application of said composition to at least one of the skin, hair, or mucous membranes, which composition comprises:

(1) an amount of at least one irritant substance sufficient to elicit an irritant side effect to a user having reactive skin when utilized in a topical cosmetic regimen that does not include the use of a substance P antagonist, wherein said irritant substance is an active agent in said topical cosmetic regimen;

(2) an amount of at least one substance P antagonist sufficient to prevent or alleviate said irritation when

said composition is utilized in a topical cosmetic regimen on a user having reactive skin, wherein said substance P antagonist is a substance which possesses at least one of the following characteristics:

(i) it exhibits a selective affinity for the NK_1 receptors on the tachykinins; and

(ii) it elicits a pharmacological response in at least one of the following tests:

(a) it reduces the extravasation of plasma through the vascular wall caused by capsaicin or antidromic nerve excitation; and

(b) it inhibits the contraction of smooth muscle induced by substance P; and

(3) a cosmetically acceptable medium;

wherein said topically applicable cosmetic composition comprises a galenic formulation which is a solution or dispersion formulated as a lotion or serum, microgranulate dispersion, vesicular ionic or non-ionic dispersion, alcoholic or hydroalcoholic aqueous solution, cream, gel, oil-in-water or water-in-oil emulsion, foam, aerosol, solid or paste.

8. A topically applicable cosmetic composition which is adapted for use in a cosmetic regimen that comprises topical application of said composition to at least one of the skin, hair, or mucous membranes, which composition comprises:

(1) an amount of at least one irritant substance sufficient to elicit an irritant side effect to a user having reactive skin when utilized in a topical cosmetic regimen that does not include the use of a substance P antagonist, and wherein said irritant substance is an active agent in said topical cosmetic regimen;

(2) an amount of at least one substance P antagonist sufficient to prevent or alleviate said irritation when said composition is utilized in a topical cosmetic regimen on a user having reactive skin, wherein said substance P antagonist is a substance which possesses at least one of the following characteristics:

(i) it elicits a pharmacological response in at least one of the following tests:

(a) it reduces the extravasation of plasma through the vascular wall caused by capsaicin or antidromic nerve excitation; and

(b) it inhibits the contraction of smooth muscle induced by substance P; and

(3) a cosmetically acceptable medium;

wherein said topically applicable cosmetic composition suitable for use in a cosmetic regimen is selected from the group consisting of a hair care composition, skin care composition, cleansing composition, sunscreen composition and a mouth care composition.

9. A topically applicable cosmetic composition which is adapted for use in a cosmetic regimen that comprises topical application of said composition to at least one of the skin, hair, or mucous membranes, which composition comprises:

(1) an amount of at least one irritant substance sufficient to elicit an irritant side effect to a user having reactive skin when utilized in a topical cosmetic regimen that does not include the use of a substance P antagonist, and wherein said irritant substance is an active agent in said topical cosmetic regimen;

(2) an amount of at least one substance P antagonist sufficient to prevent or alleviate said irritation when said composition is utilized in a topical cosmetic regimen on a user having reactive skin, wherein said substance P antagonist is a substance which possesses at least one of the following characteristics:

(i) it exhibits a selective affinity for the NK_1 receptors on the tachykinins; and

(ii) it elicits a pharmacological response in at least one of the following tests:

(a) it reduces the extravasation of plasma through the vascular wall caused by capsaicin or antidromic nerve excitation; and

(b) it inhibits the contraction of smooth muscle induced by substance P; and

(3) a cosmetically acceptable medium;

wherein said topically applicable cosmetic composition suitable for use in a cosmetic regimen is selected from the group consisting of a hair care composition, skin care composition, cleansing composition, sunscreen composition and a mouth care composition.

10. A topically applicable cosmetic composition which is adapted for use in a cosmetic regimen that comprises topical application of said composition to at least one of the skin, hair, or mucous membranes, which composition comprises:

(1) an amount of at least one irritant substance sufficient to elicit an irritant side effect to a user having reactive skin when utilized in a topical cosmetic regimen that does not include the use of a substance P antagonist, wherein said irritant substance is an active agent in said topical cosmetic regimen;

(2) an amount of at least one substance P antagonist sufficient to prevent or alleviate said irritation when said composition is utilized in a topical cosmetic regimen on a user having reactive skin, wherein said substance P antagonist is a substance which possesses at least one of the following characteristics:

(i) it elicits a pharmacological response in at least one of the following tests:

(a) it reduces the extravasation of plasma through the vascular wall caused by capsaicin or antidromic nerve excitation; and

(b) it inhibits the contraction of smooth muscle induced by substance P; and

(3) a cosmetically acceptable medium;

wherein said topically applicable cosmetic composition comprises a galenic formulation which is a solution or dispersion formulated as a lotion or serum, microgranulate dispersion, vesicular ionic or non-ionic dispersion, alcoholic or hydroalcoholic aqueous solution, cream, gel, oil-in-water or water-in-oil emulsion, foam, aerosol, solid or paste.

11. The composition of claim 3, wherein said hair care composition is selected from the group consisting of a shampoo, setting lotion, treatment lotion, hair cream, hair gel, coloring composition, restructuring lotion, permanent composition, anti-hair loss lotion and anti-hair loss gel.

12. The composition of claim 4, wherein said hair care composition is selected from the group consisting of a shampoo, setting lotion, treatment lotion, hair cream, hair gel, coloring composition, restructuring lotion, permanent composition, anti-hair loss lotion and anti-hair loss gel.

13. The composition of claim 3, wherein said hair care composition is in a galenic form selected from the group consisting of a cream, gel, emulsion, foam and aerosol.

14. The composition of claim 4, wherein said hair care composition is in a galenic form selected from the group consisting of a cream, gel, emulsion, foam and aerosol.

15. The composition of claim 3, wherein said cosmetic composition is a cleansing cream, skin protecting or skin treatment cream, make-up removal cream, foundation cream, sunscreen composition, liquid foundation, make-up removal lotion, protective or skin care lotion, skin care gel, skin care foam, bath preparation, deodorant composition, after-shave gel or lotion, depilatory cream, composition for alleviating insect sting, soap or cleansing bar.